

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Pei KAN et al. Confirmation No: 5546
Appl. No. : 10/748,192
Filed : December 31, 2003
Title : THERMOGELLING EMULSIONS FOR SUSTAINED
RELEASE OF BIOACTIVE SUBSTANCE

TC/A.U. : 1612
Examiner : Nannette Holloman

Docket No. : KANP3002/REF/LES
Customer No. : 23364

DECLARATION UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Pei Kan, hereby declare that

I am a citizen of Republic of China;

I have the following mailing address: 195, Sec. 4, Chung Hsing Rd., Chutung, Hsinchu,
Taiwan 31040, R.O.C.;

In the year 1996 I earned a Ph.D. from National TsingHua University, Taiwan;

I have been employed as a Researcher at Industrial Technology Research Institute
since 1999;

I am an inventor of the above-identified application;

I am familiar with the outstanding Office Action dated July 7, 2010, and the references
cited therein; and

My opinion is as follows:

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I reviewed PubMed on the issue of burst release of polymer microspheres. I found at least four review papers supporting the argument that a burst effect always occurs in a polymer microsphere system because drugs may reside on or close to the surface of the microsphere during emulsion-preparation. These papers were submitted with the response filed on December 7, 2010, in the present application. I assert that the presence of a burst effect in Sawhney's microspheres can be explained clearly by these review papers. It would also have been reasonable for a skilled person to expect that a burst effect must happen in Sawhney's system even if Sawhney's system is combined with Jeong's hydrogel.

Most of the papers and data cited in the review articles were published before the filing date of the present application. For example, references 1 & 2 (see below) were accepted in 2003, so all the data and cited papers had already been published before our filing date. As another example, the table of reference 3 mentions that the burst problem was reported in ref-63: "Release of recombinant human interleukin-2 from dextran-based hydrogels. *J. Control Release*. 78:1-13 (2002)."

References:

- (1) Control of Encapsulation Efficiency and Initial Burst in Polymeric Microparticle Systems. *Arch Pharm Res* 27(1): 1-12, 2004.
- (2) Polymer microspheres for controlled drug release. *International Journal of Pharmaceutics* 282:1-18 (2004).
- (3) Polymer-Based Sustained-Release Dosage Forms for Protein Drugs, Challenges, and Recent Advances. *AAPS PharmSciTech*, 9(4): 1218-1229 (2008).

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(4) Analysis of initial burst in PLGA microparticles. Expert Opin. Drug Deliv., 5(6): 615-628 (2008).

All statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine, or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the above-captioned patent.

By: Pet Ken
Pet Ken

Date: 07 Dec 08